IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

		Atty. Docket: SOLOMON1R
In re Application of:	)	Conf. No.: 3910
Beka SOLOMON	)	Art Unit: 1649
Appln. No.: 09/441,140	)	Examiner: S. L. Turner
Filed: November 16, 1999	)	Washington, D.C.
For: PREVENTION OF PROTEIN AGGREGATION	)	

DECLARATION OF BEKA SOLOMON UNDER 37 C.F.R. §1.131

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Randolph Building, Mail Stop Amendments
401 Dulany Street
Alexandria, VA 22314

Sir:

I, the undersigned Beka Solomon, hereby declare and state as follows.

I am Professor in the Department of Molecular Microbiology and Biotechnology, Tel Aviv University, Tel Aviv, Israel.

I am the inventor of the invention disclosed and claimed in U.S. patent 5,688,651 and the above-identified

patent application, which is a reissue application relating to that patent.

The application that issued as the 5,688,651 patent was filed on December 16, 1994. I conceived of the subject matter claimed in the present reissue application and communicated the conception of this invention to individuals in the United States prior to November 22, 1994. The evidence referred to herein establishes that the conception in the United States prior to November 22, 1994, was linked to the constructive reduction to practice of December 16, 1994, by reasonable diligence.

Submitted herewith in support of this declaration are declarations of Kenneth I. Kohn, Shulamit Hirsch and Roger L. Browdy. Also submitted herewith are Exhibits A-Z, referred to in one or more of these declarations.

The text of Exhibit K was sent to the United States under cover of my letter of November 2, 1994 (Exhibits B and Z) and, according to the Kohn declaration, reached the United States within two or three days following November 14, 1994, when it was sent by courier as an attachment to Exhibit F.

As per the Browdy and Kohn declarations, my *Nature* manuscript (Exhibit O) was faxed to the United States on November 16, 1994.

Thus, both Exhibit K and Exhibit O were in the United States prior to November 22, 1994, and between them contain a conception of my invention as now claimed in the reissue application.

More particularly, the first page of Exhibit O discloses the concept of the use of monoclonal antibody AMY33, which was raised against beta-amyloid fragment 1-28, to inhibit aggregation of beta-amyloid. The first paragraph concludes:

> This study provides a factual basis for the use of monoclonal antibodes as therapeutic approaches for the prevention of in vivo ß-amyloid aggregation, associated with Alzheimer's disease.

Note also the disclosure at the bottom of page 5 of Exhibit O, for the concept of developing functional small antibody fragments to serve as therapeutic chaperones for the treatment of Alzheimer's disease as well as other human amyloidosis diseases.

In Exhibit K, note the fifth page of the document, in the legend to Figure 10, where prevention of ß-amyloid aggregation by monoclonal antibody AMY 33 is disclosed. At the top of numbered page 14 (the 21st page) of Exhibit K, the following concept is disclosed:

> Once an appropriate monoclonal chaperone antibody is found or engineered, the present invention provides for its use therapeutically to prevent or reduce protein

> aggregation *in vivo*. In the preferred embodiment, the prevention of ß-amyloid aggregation is undertaken.

Note also the second paragraph on numbered page 14 of Exhibit K where the concept of use of a human antibody is set forth, as is reference to Haber, 1992, for the steps of preparing such a human monoclonal antibody. The list of references at numbered page 44 of Exhibit K shows that this is Haber, E., "Engineered Antibodies as Pharmacological Tools", *Immunological Reviews*, 130:189-212 (1992). On information and belief, this document is of record in the present proceeding and is available to the examiner. It teaches, inter alia, how to use the DNA of selected monoclonal antibodies to genetically engineer single chain antibodies and humanized antibodies.

Accordingly, this evidence establishes that my conception of the therapeutic use of monoclonal antibodies obtained using the peptide 1-28 of ß-amyloid for the inhibition of aggregation of ß-amyloid, and particularly the use of genetically engineered antibodies obtained from DNA of such monoclonal antibodies and the use of human antibodies, as well as single chain antibodies in particular, was disclosed in the United States prior to November 22, 1994.

The declarations of Kohn, Hirsch and Browdy attached hereto further establish reasonable diligence on the part of

Mr. Kohn's office in preparing and filing the patent application that was eventually filed on December 16, 1994, from a date immediately prior to November 22, 1994 (when the Anderson patent application was filed) until December 16, 1994. The evidence shows that Mr. Kohn, in the United States, received my comments on the first draft of the application within two or three days of Monday, November 14, 1994, when it was sent to him by DHL courier (Exhibit F). Furthermore, on Wednesday, November 16, 1994, Mr. Kohn received my *Nature* manuscript to review, which was directly related to the subject matter of the application (Exhibits G, N and O). It is apparent that Mr. Kohn's office worked on this application between those dates and December 2, 1994, when another draft was sent to Ramot (Exhibit P). They also worked on preparing the formal papers (Exhibits Q and R).

On December 7, 1994, Mr. Kohn's office received by fax my additional remarks and changes (Exhibit S). They subsequently worked on further revisions of the draft application, as is evidenced by Exhibits W and X, until the application was filed on December 16, 1994.

Thus, the Kohn, Hirsch and Browdy declarations and the documentary exhibits referred to therein establish reasonable diligence in the United States from November 22, 1994, to the filing of the patent application on December 16,

1994. Accordingly, my invention was made in the United States prior to November 22, 1994.

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

3/19/07
Date

/Beka Solomon/
Beka SOLOMON